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# ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE  
DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

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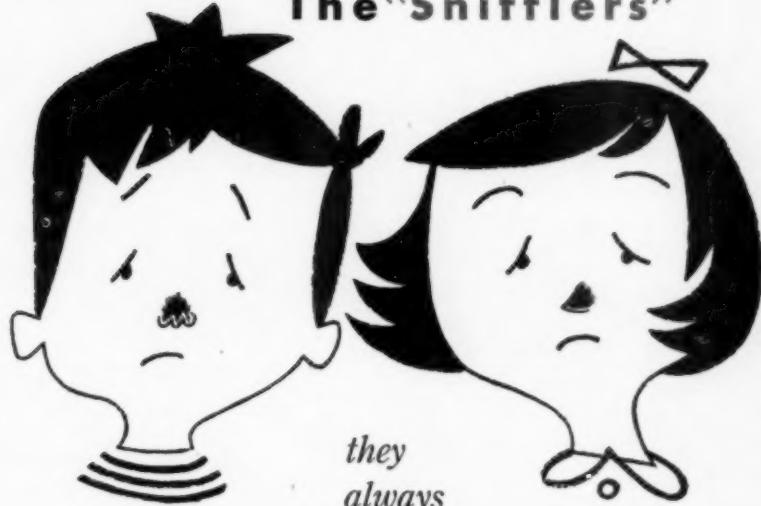
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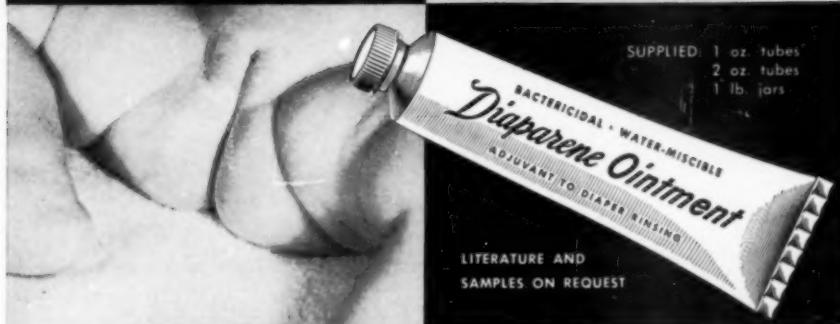
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JOHN FITCH LANDON, M.D., Editor

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## ARCHIVES OF PEDIATRICS ENTERS 75TH YEAR WITH NEW PUBLISHER . . .

The January 1958 edition of ARCHIVES OF PEDIATRICS—Volume 75—marks a new era in the uninterrupted publishing history first introduced by the January Issue of the magazine in 1884.

Albro C. Gaylor, new publisher and president of E. B. Treat & Co., Inc., brings to the journal wide experience in the publishing field.

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## AS THEY FIND IT— “PRACTICAL”

The very concise and brief clinical reports that appear in the ARCHIVES each month have been very helpful to our readers, *who have found more practical suggestions in them than in most of the long and drawn out scientific articles that appear in other journals.*

We quote from a number of letters received from subscribers:

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### Archives of Pediatrics

(Names on Application)

## STUDIES ON THE PATHWAY OF INFECTION OF POLIOMYELITIS\*

YOSHITO NISHIZAWA, M.D.

and

EIICHI MAJIMA, M.D.

Osaka, Japan.

In a previous study,<sup>1</sup> one of the authors, Nishizawa, reported that viremia occurred in poliomyelitis between the time of infection and onset of paralysis. Horstmann,<sup>2</sup> Bodian,<sup>3</sup> Jungeblut and others published reports at about the same time on the occurrence of viremia, and today viremia is accepted as a stage in the course of poliomyelitis. The various investigators, however, do not agree as to what course the virus takes to the central nervous system following the viremia stage. Jungeblut<sup>4</sup> suggests that the virus in the blood first becomes fixed in the peripheral nerves and then travels centripetally along the nerve to the central nervous system, while Bodian<sup>5</sup> proposes that the virus crosses the blood-central nervous system barrier directly from the blood stream at certain points of the central nervous system. Nishizawa has suggested the importance of the choroid plexus in regard to this problem, and on the basis of experiments on the transfer of fuchsin to the spinal fluid in experimentally infected poliomyelitis monkeys, it was theorized that the blood-cerebrospinal fluid barrier was disturbed during the stage of viremia and the virus could readily pass from the blood through the choroid plexus into the cerebrospinal fluid and then invade the anterior horn of the spinal cord. This study was conducted in an effort to verify this theory.

### EXPERIMENTAL MATERIAL

Three Java monkeys (*macaca cynomolgus*) weighing 2.0 kg. to 3.0 kg. were used in the experiments.

Virus: Type II (Lansing) virus was used in all the experiments. This virus was obtained from the Institute of Preventive Health, (Tokyo) where it had been maintained by passage in human embryo skin-muscle tissue cultures. Fluid from tissue cultures of this virus and an emulsion of the brain and spinal cord of mice

\* From the Department of Pediatrics, School of Medicine, Osaka University, Osaka, Japan.

infected with this virus were used in the experiments. The TCID<sub>50</sub> of the virus was 10<sup>-7.5</sup>.

Standard Immune Serum: The immune serum used for the neutralization tests of the isolated viruses was received from the National Foundation for Infantile Paralysis. The lyophilized serum was dissolved in distilled water just prior to use.

#### EXPERIMENTAL METHODS

Administration of Virus: Ten cc. of tissue culture fluid or 20 cc. of a 20 per cent brain-spinal cord emulsion of five mice was administered directly into the stomach of the monkey with a catheter for three successive days.

Determination of Infection: In order to ascertain whether the animal had become infected, the activity, appetite, temperature and appearance of paralysis was observed. The blood picture and cerebrospinal fluid were also examined.

Isolation of Virus from the Blood and Cerebrospinal Fluid: Tissue cultures of human embryo skin showing good five-to-seven days growth of fibroblasts were inoculated with the material. A part of the material was also inoculated intracerebrally in mice. Samples of blood were collected aseptically from the femoral vein every day from the third or fourth day to the sixth or eighth day after administration of virus. The blood was defibrinated and 0.1 cc. portions inoculated in each of the two tissue culture tubes and 0.04 cc. inoculated intracerebrally in each of five mice. Spinal fluid was collected by suboccipital cisternal tap under ether anesthesia from the fourth or fifth day to the seventh or eighth day. About 0.5 cc. was withdrawn and 0.1 cc. portions inoculated into each of two tissue culture tubes. The spinal fluid was examined in a Fuchs-Rosenthal chamber for cell count and verification of absence of red cells. The inoculated tissue culture tubes were examined once daily and the mice three to four times a day.

#### EXPERIMENTAL RESULT

Clinical Course of the Experimentally Infected Monkeys: Paralysis did not occur in any of the animals. Characteristic changes were not observed in the temperature or blood picture though a trend towards leucocytosis was noted, and in Monkey B, a rise in temperature to 39° occurred on the third and fourth day, and from about the seventh day the appetite became poor and this was

EXPLANATION OF PHOTOGRAMS—MONKEY B

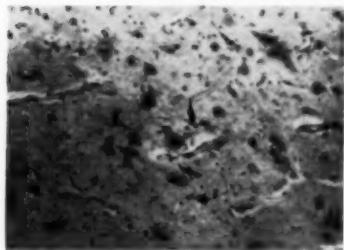


Fig. 2. Spinal Cord; Nissl's stain; marked poliomyelitic changes.

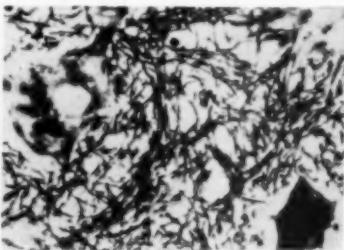


Fig. 3. Spinal Cord; Bielschowsky's stain; marked poliomyelitic changes.

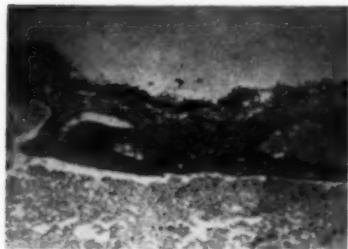


Fig. 4. Choroid Plexus; hematoxylin-cosin; degeneration and disintegration of epithelial cells and dilatation of vessels can be seen.

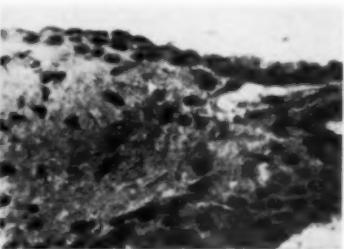


Fig. 5. Choroid Plexus; hematoxylin-cosin; swelling and edema of the connective tissue can be seen.

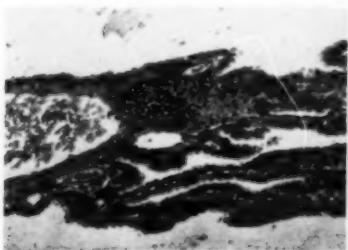


Fig. 6. Choroid Plexus; Van-Gieson's stain; invasion by inflammatory cells with formation of nests clearly visible.

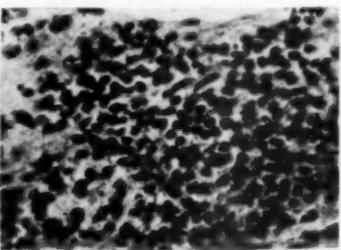


Fig. 7. Same as Fig. 6 under higher magnification.

followed by a sudden deterioration in the general condition. Monkey C showed pleocytosis of the spinal fluid (poly—16, lympho—213) on the eighth day, the day virus was successfully isolated.

**Virus Isolation:** Virus was successfully isolated from the blood (Table 1) on the fifth day in Monkey A, from the spinal fluid

TABLE 1--ISOLATION EXPERIMENT

monkey	A			B			C			
	Material	Blood	Spinal Fluid	Urine	Blood	Spinal Fluid	Urine	Blood	Spinal Fluid	Urine
Days after Oral Feeding	4	—	—	—	—	—	—	—	—	—
	5	+	—	—	—	—	—	—	—	—
	6	—	—	—	—	+	—	—	—	—
	7	—	—	—	—	—	—	—	—	—
	8	—	—	—	—	—	—	+	—	—
	9	—	—	—	—	—	—	—	—	—
	10	—	—	—	—	—	—	—	—	—

on the sixth day in Monkey B, and from the spinal fluid on the eighth day in Monkey C by cultivation in tissue cultures. Virus was not isolated from the urine.

**Typing of the Isolated Virus:** In order to ascertain that the

TABLE 2—TITRATION EXPERIMENT  
(Tissue Culture Method)

Dilution of Virus	Virus Isolated from Monkey A (Blood)	Virus Isolated from Monkey B (Spinal Fluid)		Virus Isolated from Monkey C (Spinal Fluid)	
$10^{-1}$	+++	+++	++	++	++
$10^{-2}$	+++	++	+++	+++	++
$10^{-3}$	+++	++	+++	++	++
$10^{-4}$	+++	++	+++	++	++
$10^{-5}$	++	++	+	+	++
$10^{-6}$	+	+	+	+	+
$10^{-7}$	+	+	—	+	+
$10^{-8}$	—	—	—	—	—
Control	—	—	—	—	—

+++ Marked destruction of cells.

++ Moderate destruction of cells.

+ Slight destruction of cells.

isolated virus was identical with the inoculated virus, typing tests were carried out. The isolated virus samples (Table 2) were

diluted tenfold and titrated. The TCID<sub>50</sub> was found to be 10<sup>-7.5</sup>.

**TYPING EXPERIMENT**

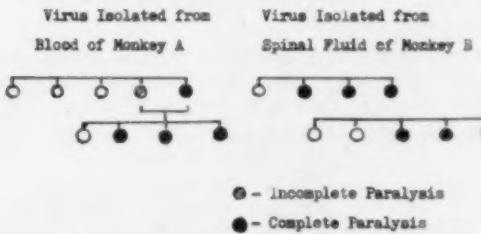
Virus	Immune Serum	Type I	Type II	Type III
Virus isolated from Monkey A (blood)		+++	-	+++
Virus isolated from Monkey B (spinal fluid)		+++	-	++
Virus isolated from Monkey C (spinal fluid)		+++	-	+++

Table 3. Neutralization tests using 100 TCID<sub>50</sub> of the virus and fivefold diluted standard immune serum showed that the isolated virus was Type II.

The virus isolated by the tissue culture method from the blood of Monkey A and the spinal fluid of Monkey B was inoculated intracerebrally (Table 4) into mice. The characteristic paralysis of poliomyelitis was observed.

**VERIFICATION EXPERIMENT**

(Intracerebral Inoculation in Mice)



Neutralization Tests of the Monkey Serum: Blood was collected prior to and 8-14 days after inoculation of polio virus. Neutralization tests were conducted with the samples against the Lansing virus using the tissue culture method but no marked rise in neutralizing antibody was found.

Histopathological Findings: Monkey A was sacrificed on the tenth day and Monkey B on the eighth day by exsanguination (heart puncture) under ether anesthesia. The organs were studied histologically and the following observed. Typical poliomyelitic changes were present in the stomach, intestines and liver of the animals. The spinal cord (Table 5) was stained with Nissl's stain

and changes typical of poliomyelitis as degeneration and disintegration of the nerve cells, neuronophagia, dilatation of the vessels and proliferation of glia cells were found. Bielschowsky's stain too showed atrophy of the cells, increased stainability, swelling of the cell body, vacuolization and reduced stainability of the cytoplasm. In other words, a picture of imminent paralysis was present.

#### HISTOPATHOLOGICAL CHANGES IN THE SPINAL CORD

Site	Findings	Monkey A	Monkey B
Cervical Cord	Degeneration of Neurons	++	++
	Disintegration of Neurons	+	+
	Neuronophagia	±	±
	Dilatation of Vessels	+	+
	Proliferation of Glia Cells	+	+
Thoracic Cord	Degeneration of Neurons	+	++
	Disintegration of Neurons	±	+
	Dilatation of Vessels	±	±
	Proliferation of Glia Cells	±	±
Lumbar Cord	Degeneration of Neurons	++	++
	Disintegration of Neurons	+	+
	Neuronophagia	+	++
	Dilatation of Vessels	+	++
	Proliferation of Glia Cells	+	+

Degeneration consists of atrophy, swelling of cell body, karyolysis of Nissl's body, abnormal staining of nerve fibers and disruption of the course of the fibers.

The changes in the choroid plexus (Table 6) were examined particularly in detail. Staining was by hematoxylin and eosin and

TABLE 6. HISTOPATHOLOGICAL CHANGES  
IN THE CHOROID PLEXUS

		Monkey A	Monkey B
Degeneration of Epithelium		+	+
Inter- stitium	Edema	+	+
	Dilatation of Vessels	+	+
	Swelling of Connective Tissue	+	+
	Inflammatory Cell Infiltration	+	++

Inflammatory cells—chiefly monocytes and lymphocytes, also some polymorphonuclear cells and eosinophiles in places.

Van-Gieson. Degeneration, disintegration and separation of the

epithelial cells were found. The nuclei were pyknotic in many of the cells and even destroyed in some while the cell body was swollen and enlarged and contained many large and small vacuoles. The interstitium showed dilatation of the vessels and edema with swelling of the connective fibers. Infiltration by inflammatory cells was also observed. That is, groups of monocytes, lymphocytes and at times eosinophiles were observed scattered in places and as can be seen in the photographs, nests of infiltration were present. These nests were composed for the most part of monocytes and lymphocytes but some eosinophiles and neutrophiles can also be seen.

#### SUMMARY

Polio virus was successfully isolated from the cerebrospinal fluid of two monkeys, six and eight days after oral infection and from the blood of one monkey on the fifth day. All the animals were studied histopathologically and typical changes of poliomyelitis were found in the spinal cord and other organs. The choroid plexus in particular showed marked infiltration by inflammatory cells with formation of nests. From these results it is suggested that the virus in the blood passes through the choroid plexus and enters the central nervous system. The isolation of polio virus from the spinal fluid during this period appears to substantiate this theory. The neural pathway as well as the hematogenous pathway are, of course, possible routes by which the virus may reach the central nervous system but it is believed that the route via the choroid plexus is worthy of consideration.

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THE MILK AND WATER INTAKE OF  
SMALL CHILDREN\*  
A Survey of Drinking Habits.

H. H. NEUMANN, M.D.

New York.

The introduction of fluorides into the drinking water has created interest in the quantitative aspects of the daily consumption of drinking water per se, particularly by children, and in the range of variation from the average intake. A search of the literature offered little information on this topic. Some of the figures occasionally quoted, as those by McClure<sup>1</sup>, are based on assumptions and calculations rather than on actual histories. Statements like "the intake of water, though it may be somewhat irregular is less variable than other items in human nutrition" (Pearlman<sup>2</sup>) appear in the literature without reference and evident foundation in fact. Comparing the water and milk intake it has been stated (Doty<sup>3</sup>) that the milk consumption of children varies to a much larger extent than the intake of tap water.

Since no data were found in the literature referring to any surveys, comparing the intake of tap water and of milk or other fluids by children, and since it may seem to the experienced pediatric nutritionist that the milk intake of the American child is subject to relatively moderate variations, while on the other hand there are large differences in their water drinking habits, it was attempted to probe into this subject by taking the histories of the drinking habits of preschool children living in suburban Long Island. Attention was focused chiefly on the specific sources of liquids taken by drinking and not on those naturally contained in "solid" foods. While the obtained answers seemed to follow a certain standard pattern, the possibly great variability of such figures in different climates and environments and even with changing vogues must be kept in mind.

In order to determine current customs and practices of furnishing fluids to small children, detailed histories were taken regarding the drinking habits of 312 children below the age of six years.

\* From the Laboratory of Dental Research, School of Dental and Oral Surgery, Faculty of Medicine, Columbia University, New York.

The histories were obtained from the mothers who were definite and unhesitant in relating the amounts used daily, since they usually control closely the feeding and drinking at this age.

The method of survey by questionnaire has, of course, its limitations and is admittedly subjective. Yet an institutional study to obtain such data may not apply to the habits found in private homes, and any methodical measurements carried out by hundreds of individual mothers may introduce other and larger variables difficult to control, aside from the possible interference with the spontaneity of the selection. The same set of prepared questions was presented to the mothers and the answers as given in household measures were noted by the interrogator. The results of the present inquiry followed a pattern which can be summed up as follows.

#### TOTAL FLUID INTAKE BY DRINKING

The fluids consumed daily, with varying regularity, and by drinking, are provided to a large extent by dairy milk and tap water, that is, the average intake of milk and tap water per se combined was 1136 cc.

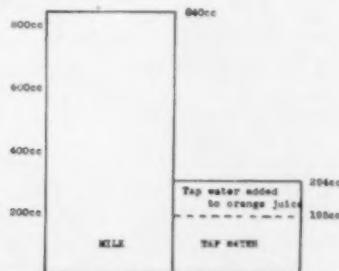


Fig. 1. Average daily intake of dairy milk and tap water per se, below age six.

The histories were grouped into three age levels. In the following presentation they are combined, with subsequent reference to the differences at the various age levels.

These 1136 cc. constitute the bulk, though of course not the entire fluid intake; more is derived from fruit and vegetables composed of over ninety per cent of water, from the cooked and "solid" foods containing often sixty and seventy per cent water, and other beverages besides milk and tap water, which are referred to later.

Water of oxidation from the ordinary mixed diet furnishes an additional eight per cent to ten per cent of the total water requirement<sup>4</sup>.

#### MILK

In the questioned group, the principal source of fluids of the children from six months to five years was dairy milk, with an average consumption of 840 cc. (over 1½ pints) per day, and with little variation if broken down to smaller age groups.

Less than three children in a hundred had been breastfed for any length of time in this area. It appears that the infant formula, made up of milk, tap water and some carbohydrate, had been discontinued at somewhat earlier ages than textbooks would suggest, usually at an age of three to four months. Children on formula after the age of four months were the exception. Among the 312 children under question no case of allergy to cow's milk was reported; all the children drank dairy milk.

If the children were graded according to the amount of their milk consumption, the third representing the heaviest drinkers consumed an average of 1005 cc. and the lowest third an average of 647 cc. per day; the deviation from the mean is notably small with a ratio of 1:1.5 between the low third and top third of milk drinkers.

#### TAP WATER

The average drinking water intake was 294 cc. per day. The quantities were obtained in commonly used household measures and were converted into cubic centimeter to calculate averages. Dividing the children again into three groups according to their water consumption, the lowest third consumed an average of 85 cc., while the mean intake of the upper third, that is of the heavy water drinkers, was 618 cc. Twenty-nine per cent of the mothers claimed that their small children never or hardly ever drink tap water *per se*. The addition of water to frozen orange juice and its widespread use has somewhat altered this picture, and the amounts thereby used are referred to later. At the other extreme, a proportionately much smaller group of children were described as heavy water drinkers.

In contrast to the milk intake, the water consumption varied

widely, at a ratio of 1:7.4, relating the mean of the lower and of the upper third.

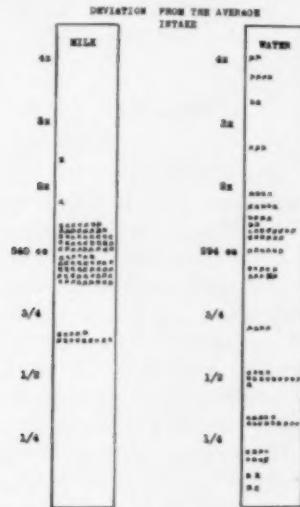


Fig. 2. Each X represents 1% of the children. The scattering in groups is influenced by the size of the more commonly given household measures. 840 cc. for milk, and 294 cc. for water, represent the averages. Attention may be drawn to the non-linearity of the scale above and below the average, and that the tables would have to extend considerably above the median figure for an undistorted portraying of the scattering.

## FRUIT JUICES

Outside of milk and water, the only other fluid consumed habitually and regularly was orange juice; 66 per cent of the children drank prepared frozen orange juice, 26 per cent fresh juice, while 8 per cent did not drink orange juice. As frozen juices are prepared with tap water at a ratio of 3:1, the water contained in prepared juice was included in the charted figure (1) for water intake. The average amount of tap water consumed daily with frozen orange juice was 99 cc. Other juices as apple, tomato, and grape juice were rarely used with great regularity, and amounted percentagewise to only a small fraction of the total liquid intake.

## **SOFT DRINKS**

The average consumption of carbonated drinks was low in this

age group. As most drinks were handed by the mother, it is easy for her to control the intake of soft drinks. In contrast to older children and possibly to other areas only one small child in thirty-five in this area was allowed carbonated drinks daily and with any regularity.

#### COOKED FOOD

Queries on the intake of water in cooked food showed the amounts to be as widely variable as for drinking water, however, on a much lower quantitative level, thereby not altering essentially the total picture. Tea and coffee as beverages were of no significance at this age. Soups prepared with water were taken daily only by one child in forty. Generally soups were given irregularly and infrequently and played a minor role in the liquid intake of the preschool child; sauces and gravies were hardly used. Fresh fruit, vegetables and meat which contain structurally a high percentage of water do not seem to absorb water during preparation; weighing some staples—vegetables, potatoes and meat—before and after cooking revealed no weight increase, rather a slight, varying weight loss. Tap water is absorbed during the preparation chiefly by dehydrated foods, some cereals, and jello. As aforesaid, the total amount of water thereby consumed varied greatly, though on a much lower average level. Since the prevailing tendency is to use milk with cream soups, desserts and ready-for-use cereals, to broil food and to use pressure cookers with a minimum of water, the tap water consumption with cooked food appears proportionately small.

#### OTHER VARIABLES

During hot weather, that is, during a relatively short period of the year in this region (for a 2-3 per cent of the hours in a year when the temperature exceeds 80°F. on Long Island) the fluid intake is affected; no attempt was made to obtain quantitative information for this period. Part of the additional consumption is provided by the previously mentioned fruit juices, that is orange, apple, tomato and grape juice in that order.

The histories were grouped according to age levels. In the presentation the figures were combined since breaking them down to smaller age groups showed an equally wide variation in the water intake from infancy to age five years and little change in the milk

consumption, that is, a child aged six months is as likely as a child aged six years to consume over one and one half pints of milk daily. An infant weighing 5 kg. consumes daily close to 1000 cc. or 20 per cent of its body weight in liquids. This percentage decreases steadily to 2-3 per cent in the adult. The fluid requirement at age one being approximately 1200 cc. and at the age of five 1500 cc. per day, the increase in the fluid demand of the heavier and older child is somewhat balanced by the decreased liquid requirement per kg. bodyweight.

#### DISCUSSION

It would be of interest to compare the milk and water drinking habits of the young child in this area with other geographic and particularly climatic areas. Even though in this region the tap water consumption seems to vary widely, much more so than milk consumption, it is not intended to debate in this connection the merits of water or milk fluoridation since other factors are involved in the issue. However, a presumed "constancy of water consumption" against a "high variability of milk intake" should be avoided as criterion since this belief is not based on available data and seemingly not founded on facts.

Widdowson (1947) who examined the diet of English "middle class children", aged one to eighteen, found that similar individuals may "differ enormously and unpredictably in their food habits"; the milk intake in the lower age group, however, was fairly constant with an average of nineteen ounces per day in the one-year-olds, and eighteen ounces in the six-year-olds; these figures, though slightly lower than the findings on Long Island, are of a similar general order.

#### SUMMARY

1. The average milk intake of 312 Long Island children under the age of six was found to be 840 cc. per day. The deviations from the average were small, with a ratio of 1:1.5 between the mean of the lower third and the top third of milk drinkers.
2. The average intake of tap water including water added to frozen fruit juices was 294 cc. The consumption varied at a ratio of 1:7.4, relating the mean of the lower and upper third of water drinkers.

3. The only other fluid given commonly and regularly, to 92 per cent of the children under question was orange juice. Sixty-six per cent of the children drank frozen orange juice prepared daily and 26 per cent fresh juice. The average amount of tap water consumed daily with frozen orange juice was 99 cc.

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TWO CASES OF SCLERODERMA IN PREMATURE INFANTS CURED BY SUBCUTANEOUS INJECTIONS OF HYALURONIDASE. (Gass, Med. Ital., 113:321-322, Oct. 1954). Twin brothers born at the eighth month of a pregnancy, weighing 2,450 gm. and 2,400 gm., respectively, were seen by the author the first week after their birth. The clinical findings—edema; tightness and hardening of the skin, especially that of the feet and legs; coldness (rectal temperature less than 34 C.) ; a weak cry; and inability to suck—were characteristic of scleroderma. There was no family history of scleroderma. Hot water bottles about the infants and administration of analeptic agents, Simpamina D ( a form of amphetamine) and penicillin were ineffectual. After 48 hours of this regimen the condition was unchanged, and the edema was extending while the skin was hardening. Hyaluronidase was then resorted to. It was injected subcutaneously in small doses of 0.1 to 0.2 cc. (about 8.5 to 17 viscosity units) at 1 to 3 cm. from the involved areas, depending on the intensity of the sclerosis, for a total dose of 125 viscosity units the first day and 250 every day thereafter. The injections were performed for three days in the heavier infant, whose general condition was better than the brother's, and for five days in the other. There were no side-effects, and both infants made a complete recovery. At the time of writing, three months after the treatment, both had survived severe attacks of influenza with bronchitis and fever.—J.A.M.A.

## EVALUATION OF A FORTIFIED MULTIVITAMIN FORMULA AS A SUPPLEMENT TO FEEDING IN NEWBORNS AND EARLY INFANCY

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In the past quarter century, there has been increasing recognition of the need for and benefits of vitamin supplements in the diets of infants. Two or three decades ago it was a growing practice to use a source of vitamins A and D, usually cod liver oil, and a source of vitamin C, usually orange or tomato juice. It soon became apparent that this supplementation was not adequate to maintain optimal function and growth. Increasingly, studies showed that nutritional deficiency in pregnancy, and especially in the later months of pregnancy, was more the rule than the exception (Tompkins<sup>1</sup>). Thus, many infants are born with nutritional deficiency, and as lactation imposes even a greater metabolic drain on the mother than pregnancy, many nursing infants have progressive vitamin deficits. For those on formulas, in which heat, the addition of processed foods and the like, diminish the vital nutritive quality of the diet, nutritive inadequacy is even more common.

With progress in knowledge of nutrition, more and more of the known micronutrients have been shown to be essential to healthy human growth and development. Recently, efforts have been made to promote the thesis that vitamin supplementation is unnecessary and that commonly available foods contain an abundance of all the factors necessary for health. This is contradictory to numerous studies of the last two decades on the nutrition of adolescents and adults which demonstrated that normally consumed foods fail to maintain healthy cellular metabolism in a great many persons, and certainly could not restore vitamin deficits already in evidence. These studies indicate a definite need for vitamin supplementation.

Accordingly, this investigation was undertaken on two comparable groups of infants to determine the relative effects of supplementation with vitamins A and D only (as still widely practiced) as against supplementation with a preparation containing these factors plus thiamine, riboflavin, niacinamide, pyridoxine,

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panthenol, choline, betaine, inositol, vitamin B<sub>12</sub>, ascorbic acid and vitamin E.\*\*

#### PATIENT MATERIAL AND METHODS

This study was undertaken in a maternity hospital and in a well baby clinic. Of a total of 545 cases originally included in the investigation, complete records were available for review at the end of eighteen months on 145 cases. Only the latter, therefore, were included in the final tabulations.

There were 81 infants (60 males and 21 females; 73 white and 8 negro) who received fortified multivitamin drops (Group A). The control series (Group B) comprised 64 infants (37 males and 27 females; 58 white and 6 negro). These infants received supplements of vitamins A and D<sub>3</sub> only. Vitamin C was invariably supplied in the form of fruit juices as part of the diet. All were followed through private facilities and well baby clinics. These patients all lived in different neighborhoods, and thus each group provided a fair cross section of different economic levels.

Both groups received identical house formulas in the nurseries and the same formulas and feeding routine throughout the study. The babies were examined at monthly intervals during the first twelve months, and more frequently when it was advisable. In many instances a powdered whole milk was supplied in lots sufficient for two weeks (for the first six to nine months). If other milk formulas were used, the total calories were the same. The vitamins were also supplied through the clinic and the patients were weighed and measured and blood counts taken at regular intervals. Each infant, unselected, received on an alternate basis 0.3 cc. either of the vitamin A and D mixture (Group B) or of the fortified vitamin drops (Group A) for the first month, then 0.6 cc. for the remainder of the study. The composition of the vitamin supplements is given in Table 2.

#### WEIGHT

The weights of all the infants in both groups were taken at regular intervals. The comparison is graphically demonstrated in the curves in Figure 1.

\*\* Vi-Syneral Vitamin Drops Fortified for this study was supplied by the U. S. Vitamin Corp., New York City.

CHART 1

FORTIFIED MULTIVITAMIN DROPS		CONTROL CASES (A & D ONLY)	
(Group A)		(Group B)	
	Average Lbs.		Average Lbs.
Birth Weight	7	7	
Discharge Weight	7	6.8	
1 month	8.2	7.9	
3 months	12	11.5	
6 months	16.5	16	
12 months	23.3	22.7	
18 months	28.5	25.3	

## HEIGHT OR BODY LENGTH

Body length measurements were taken only at regular intervals for the first six months, in both studied and control groups. The average body length, at the end of six months, of the 56 babies in Group A was 26.3 inches, while that of the control Group B (based on 33 babies) averaged 25.10 inches. Because the measurements in both groups were not taken routinely at later examinations, body length comparisons beyond six months of age were not made.

## HEMOGLOBIN

The hemoglobins were taken at regular intervals. The results were compiled and averages are shown in Chart 2 and in the bar graphs in Figure 2.

CHART 2

FORTIFIED MULTIVITAMIN DROPS		CONTROL CASES (A & D ONLY)	
(Group A)		(Group B)	
	Average		Average
3 months	72.42%	70.31%	
6 months	76.18%	—	
1 year	79.68%	69.48%	
18 months	83.27%	70.53%	

The vitamins used in both groups were as follows:

Group A: Fortified multivitamin drops (flavored).  
Group B: Vitamin A and D<sub>3</sub>.

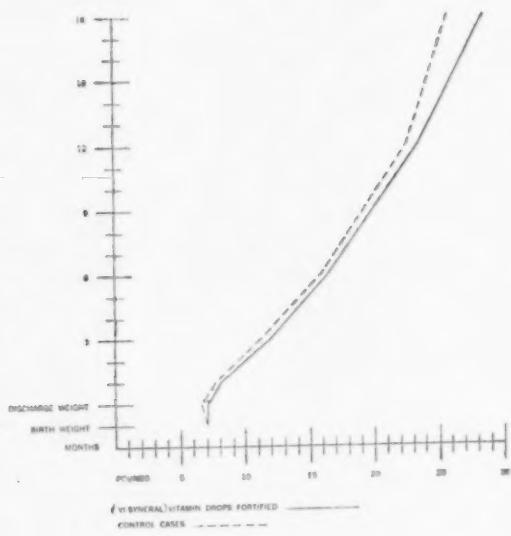


Fig. 1.

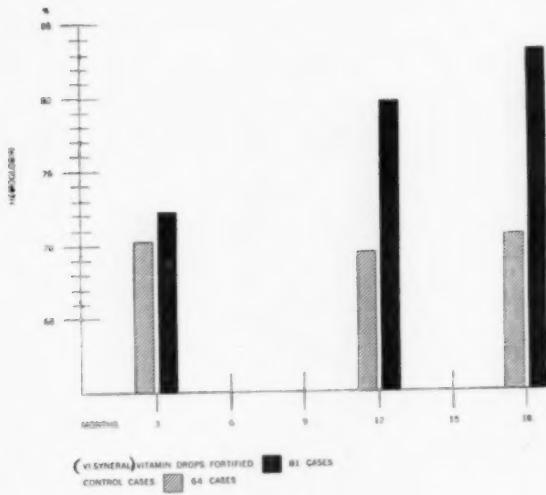


Fig. 2.

Here we can see a sharp contrast. There are important differences in the comparative graphs of both groups. At the end of three months, the group receiving the fortified multivitamins (Group A) had an average hemoglobin of 72.4 per cent as against 70.3 per cent in the controls (Group B). At one year, the hemoglobin in Group B was 69.48 per cent compared with 79.68 per cent in Group A. At 18 months, the contrast was still more marked, 70.53 per cent in the control group to 83.3 per cent in the fortified multivitamin group. This is a very marked and significant difference.

#### DISCUSSION

What stands out from this study is the fact that vitamin supplements not only prevent deficiencies in the newborn but aid in the development of healthy babies, establishing a solid foundation for the future. The superiority of a multivitamin formula over vitamins A and D alone supplemented with vitamin C in the diet was striking. This is not surprising in view of what the literature reveals as to the metabolic functions of the additional components of the more complete mixture. Thus, addition of supplemental vitamin C up to 50 mg. per day, for instance, increases the absorption of iron<sup>2</sup> in normal subjects and in those with hypochromic anemia from a level of 3 per cent to 5 per cent to one of 20 per cent to 75 per cent<sup>3</sup>. It also prevents scurvy, the megaloblastic anemia of infancy, as well as iron deficiency anemia. Ascorbic acid acts as a respiratory enzyme or co-enzyme to serve as a hydrogen transport between unidentified metabolites. It has been the practice of many clinicians<sup>4</sup> to increase the daily intake of vitamin C as it had been observed that infections as well as drugs, for example, aspirin<sup>5</sup>, rapidly deplete the tissues of this vitamin.

Although fresh orange juice, providing natural vitamin C, is one of the best sources, allergic reactions and its not infrequent tendency to produce digestive disturbances<sup>6</sup> or gastrointestinal conditions that interfere with adequate absorption, often prevent the use of this natural source of ascorbic acid.

There is no question as to the importance of the B complex vitamins for their vital functions in enzyme systems and in a variety of metabolic processes. Minimum requirements for thiamine, riboflavin and niacin have been determined by urinary excretion tests in infants fed purified diets, similar to those used in experimental

animals. It was found in preliminary studies that neither breast milk nor cow's milk always provides an adequate margin of safety<sup>7</sup>.

Recently, Eliot<sup>8</sup>, Molony and Parmelee<sup>9</sup>, and Coursin<sup>10</sup> reported clinical observations on infants who received a commercial milk preparation low in content of vitamin B<sub>6</sub>. These infants had evidence of involvement of the central nervous system manifested by hyperirritability and convulsions. In animal experimentation, prominent signs of deficiency include decreased rate of growth, anemia, and a decrease in circulating lymphocytes<sup>11</sup>. It must be noted that the milk diet of infants is usually low in vitamin B<sub>6</sub>, more so than the diet of the older child. Consequently, the incidence of hyperirritability and seizures is higher in infants. Adequate protection from birth with vitamin B<sub>6</sub> is essential. The daily amount taken in fortified vitamin drops,<sup>\*\*</sup> together with the amount in the food, is sufficient to overcome any deficiencies. Lejkovsky and associates<sup>12</sup> found that vitamin B<sub>6</sub> participates in a wide variety of the enzyme systems, and in the metabolic utilization and transformation of amino acids. Most significant reactions are decarboxylation and transamination. Deficiencies of vitamin B<sub>6</sub> manifest themselves metabolically in disturbances of amino acid, and thus of protein metabolism, which can be extremely serious in a rapidly-growing organism.

Wetzel and associates<sup>13</sup> have shown that vitamin B<sub>12</sub> supplementation was followed by increased growth in children whose growth was below standard as measured by Wetzel's grid records. Two precepts of the modern treatment of undernutrition in infants and children coincide with the principles on which the grid technique of evaluating their physical condition and their growth and development has been based. Emphasis is placed today on treating the child rather than the disease, and as a distinct individual rather than as a replica of some average child. In my study<sup>14,20</sup> of vitamin B<sub>12</sub> in 324 newborn infants over a period of three years, the weight and height curves of infants on B<sub>12</sub> were definitely increased as compared with controls.

This is illustrated also in our present study. It may take many months for this phenomenon to be manifest, as evidenced in our study by a sharp rise in growth as compared with the controls only after approximately 18 months supplementation with the fortified vitamins.

Mason<sup>15</sup> has pointed out that tocopherol concentration is low in

the tissues of the fetus and newborn and considers that this "precarious tocopherol status" may provide a basis for a deficiency state during infancy and early childhood. Gordon and Nitowsky<sup>16</sup> and Wright, et al.<sup>17</sup> emphasize the low tocopherol content of most artificial formulas for infants compared with that of breast milk.

Stone<sup>18</sup> has reported that vitamin E therapy produced an improvement in muscle tone and general health in apparently normal children with retarded muscular development.

Lipotropic choline, inositol and betaine are factors concerned with the transport and deposition of fat and more indirectly with carbohydrate and protein metabolism. Deficiency of choline produces marked accumulation of fat and other lipids in the liver and degenerative changes in the kidney and coronary arteries. When young rats are subjected for only five days to a diet deficient in choline and its precursors and are then returned to a full normal diet, a malignant hypertension develops in later life.<sup>19</sup>

#### SUMMARY

A comparison was made of the effects of supplementing infants' diets with vitamins A and D alone as against a more complete supplement containing, in addition to A and D, important B complex vitamins, lipotropic factors, ascorbic acid and vitamin E (Fortified Vitamin Drops).

The infants were studied from birth to 18 months. In a group of 81 which received the fortified multivitamin drops, the average body weight at 18 months of age was 3.2 pounds more, and the average hemoglobin level 2. gms. per 100 cc. higher (an increase of more than 18 per cent) than in the control group of 64 babies who received only vitamins A and D. The diets for both groups were otherwise similar, and previously considered adequate nutritionally.

The fact that in the control group (given vitamins A and D only as a supplement) the average hemoglobin did not rise above 10.9 gms. per 100 cc. (70.5 per cent) demonstrates the inadequacy of current infant dietaries. Supplementation of the dietaries with a more complete vitamin mixture brought the hemoglobin to 12.9 gms. per 100 cc. (83.3 per cent). This study corroborates evidence from other sources for the need to supplement the infant's diet with as complete a vitamin mixture as possible.

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## BILATERAL WILMS' NEPHROBLASTOMA. G. B. Doyle (Arch. Dis. Childhood, 31:51-52, Feb. 1956).

Doyle reviews the literature on bilateral Wilms' nephroblastoma and reports a case of a three-year-old girl who took a fall while playing in the road. Radiographs at the time of this mishap showed no abnormalities. In the next two months she had occasional bouts of vomiting, and her mother noticed a gradual enlargement of the abdomen. Urinary examination showed a few red blood cells in the uncentrifuged specimen. A roentgenogram of the abdomen showed a large opacity due to a mass of soft tissue. Shortly afterwards the child went into extreme shock and collapsed. An abdominal paracentesis was performed, and about half a pint of straw-colored fluid was aspirated. The patient's condition slowly deteriorated and she died. The abdomen contained a large tumor mass in the region of each kidney. Sections of both tumors showed the typical pattern of Wilms' nephroblastoma. The rarity of bilateral Wilms' tumor suggests that such cases as do occur are usually multifocal in origin and that direct extension from one kidney to another is unusual.—J. A. M. A.

## THE TREATMENT OF FOURTEEN MENTALLY RETARDED BOYS WITH SPARINE\*

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and

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We have reported our observations of mentally retarded children under treatment with thorazine.<sup>1</sup> We were interested to compare the results with those found when other tranquilizing drugs were used. Sparine,<sup>†</sup> chemically related to thorazine, is believed to be even less toxic than thorazine. We, therefore, observed some children under sparine in the same way we had done with thorazine.

There are various publications concerned with the tranquilizing effect of sparine in psychotic or overactive patients and alcoholics. These showed good results without any adverse side effects.

Fazekas, Schultz, Sullivan and Shea reported an experiment with sparine.<sup>2</sup> Promazine was administered to 407 acutely disturbed patients, including 103 psychotics, 42 addicts, and 202 alcoholics. The dose was 50 mg. to 400 mg. daily. There were none of the complications reported after the use of other phenothiazine derivatives. Medical and nursing problems were considerably reduced. The authors stated that the drug was effective in inducing sleep and maintaining the subjects in a quiescent, detached state. Patients were readily aroused from sleep to care for their personal needs.

Mitchell<sup>3</sup> also reported on one hundred and forty-one patients, hospitalized for acute alcoholic intoxication, who were treated with sparine. Seventy per cent also were suffering from various complications. Dizziness and postural hypotension were the only side effects encountered. The author concluded that results were more satisfactory than those with a similar group treated with thorazine.

Frederick LeMere<sup>4</sup> treated 75 psychotic patients with sparine, and with the exception of chronic psychotic patients, maximum

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†The Sparine (promazine) for these experiments was supplied by the Wyeth Company, Philadelphia, Pennsylvania.

TABLE I. CLINICAL DATA ON 14 PATIENTS IN STUDY OF EFFECTS OF SPARINE THERAPY

Name	Age	I.Q. before Experiment	Diagnosis	Behavior before Sparine Treatment	Behavior after Sparine Treatment	Results in Terms of Manageability
K. B.	15	.63	Familial	Destructive, quarrelsome, odd, sadistic	A slight improvement; quieter	Fair
A. C. (twin)	14	.79	Familial	Runaway, hyperactive, destructive, distractible	A slight improvement	Fair
J. C. (twin)	14	.70	Familial	Runaway, hyperactive, distractible	Improvement; trying hard	Good
M. C.	13	.45	Idiopathic	Temper tantrums, assaultive, lazy, untidy	No improvement	None
L. C.	13	.75	Familial	Aggressive, quarrelsome, runaway, not dependable	Some improvement	Fair
E. Dr.	15	.73	Familial	Stubborn, disobedient, untidy	Some improvement	Fair
E. Du.	13	.61	Familial	Destructive, distractible, emotionally unstable, satisifc, noisy	Improvement	Good
R. G.	16	.70	Idiopathic	Fire-setting, hyperactive, stubborn	Some improvement	Fair
R. O.	20	.53	Idiopathic	Quick-tempered, destructive	No improvement	None
J. R.	16	.63	Idiopathic	Runaway, mischievous, untrustworthy, destructive	Improvement	Good
F. S.	13	.54	Familial	Runaway, destructive, emotionally unstable	No improvement	None
E. Th.	18	.44	Familial	Denialistic, hyperactive, destructive	Improved	Good
E. To.	14	.61	Idiopathic	Stubborn, secretive	Improvement	Good
D. W.	14	.73	Familial	Untrustworthy, profane, runaway	Improvement	Good

effectiveness was obtained in a day or two. The writer noted that promazine was remarkably free from side effects.

Usdin<sup>5</sup> treated 30 agitated depressive cases in private office consultation with sparine. Twenty-three of these patients were obviously improved, many of them by the second or third day. Other tranquilizing agents had been tried without improvement.

Figurelli<sup>6</sup> treated 54 alcoholics with promazine whose ages ranged from 24 to 74 with a median of 49. Daily dosage totalled 400 mg. administered by mouth. Most of the patients became quiet at once and fell into a sound but not stuporous slumber. Unless prevented by a complicating illness all were able to return to work after discharge. There were no side effects. This experiment was undertaken to find a substitute for thorazine in those patients in whom thorazine produces an undesirable change in the blood picture or has other undesirable side effects.

*Procedure.* Fourteen hyperactive boys were treated with sparine. Ages, I.Q. ratings, and diagnoses are listed in Table I. Sparine (promazine) was given orally. The therapy started with small doses such as 25 mg. twice daily, then was increased to 200 mg. according to the individual response. The experiments were started on November 9, 1956 and ended December 27, 1956, a total of 49 days.

Drowsiness was the principal side effect. This was noted in all but one case at the time of the final psychological examination. Three patients complained of anorexia, one of a burning feeling in the stomach, and two of vomiting, but these were temporary reactions. Morning temperatures were taken during the experiment and the majority showed a tendency to hypothermia. A blood count was taken before, during and after treatment and showed elevation of leukocytes and this remained after treatment in the majority of patients, probably the result of upper respiratory infection.

Matrons and teachers were asked to describe behavior and work before and after therapy. Data are shown in Table I.

*Results.* The results were good in six cases, fair in five cases. There was no improvement in three cases.

The following tests were given to experimental and control cases both before and after therapy.

1. Revised Stanford-Binet for Intelligence, Form L.

2. Picture Completion from the Wechsler Intelligence Scale for Children.
3. Picture Arrangement from the Wechsler Intelligence Scale for Children.
4. Block Designs from the Wechsler Intelligence Scale for Children.
5. Object Assembly from the Wechsler Intelligence Scale for Children.
6. Coding from the Wechsler Intelligence Scale for Children.

On the Revised Stanford-Binet the experimentals gained 2.1 I.Q. points, on the average, as compared with 0.6 I.Q. points (six-tenths) for the controls. However, the difference was not statistically significant. Likewise, differences in the Picture Completion, the Block Designs, the Object Assembly, and the Coding tests were also without significance.

On the picture arrangement test, however, the *controls gained more* than the experimentals, and the results were significant at the 5 per cent level. Four of the experimentals showed a loss on this test, whereas none of the controls showed a loss. Since the picture arrangement test is a test of social alertness, it appears that for our subjects sparine affects social alertness adversely. This result is not surprising since according to theory tranquilizing drugs are likely to make persons less sensitive to their surroundings.

In conclusion, we may say that the results of our experiments were similar to those with thorazine. Improvement in behavior occurred in 43 per cent of our cases. There was no significant gain in I.Q. ratings. On a test of social alertness, the *experimentals gained less* than the controls.

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## PEDIATRICS AT THE TURN OF THE CENTURY

*From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.*

### INTESTINAL INTOXICATION IN INFANTS\*

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In selecting this well-worn theme for my subject, I feel that I owe this society an apology inasmuch as several years ago I presented to you a paper on the same general subject. But as my experience widens I find this topic more engrossing, and I am more and more impressed with the feeling that our knowledge of it is still inadequate and that we are just at the threshold of a door that will open up new and rich fields of investigation as our knowledge of physiological chemistry increases, so that many things now obscure and imperfectly understood will become clearer.

To one whose work is largely among children, this question of intestinal poisoning is of paramount importance because it is fraught with much greater danger than a similar condition in adults. I shall attempt to deal with this matter from a practical and clinical point of view only, as my knowledge of its chemistry and bacteriology is very meagre. Also, I shall not attempt to cite any authorities, although the medical literature of the present teems with contributions on this subject. I shall discuss cases drawn from my own experience, my own conclusions in regard to, and my own methods of treating, them. I do not wish to claim originality in any of these particulars. I am dealing with a very familiar subject. Yet I feel that it is not understood as it should be by the generality of medical men for I meet practitioners very often who do not at all grasp the situation, and I am sure that many lives are sacrificed to ignorance of a matter that should be universally understood. This is no doubt partly due to the fact

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\*\* At the time of writing this paper, the author was Attending Physician, Babies' Hospital, New York.  
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that few text-books seem to consider it important enough to merit more than brief mention.

I should like to preface my remarks by a brief statement of my position in regard to acute intestinal poisoning. I believe that it is the cause, in little children, of more serious results than any other single factor, that its results are very subtle and far-reaching. I have often seen babies die in a short time from this cause alone. There is no doubt that many supposititious cases of meningitis, cerebral hemorrhage and other grave cerebral conditions are due to intestinal reflexes alone, and that the serious possibilities of milk intoxication are only beginning to be understood.

In speaking of intestinal intoxication, I do not include cases accompanied by diarrhea. This is too wide a field and is generally quite well understood. In these cases the diarrhea is an effort of nature toward spontaneous cure and is entirely conservative. I have in mind only instances in which the poison is locked up in the bowel and in which absorption is rapid and dangerous. There seems to be no effort to get rid of the poison, and it is often extremely difficult, and sometimes impossible, to stimulate the gut to empty itself. Whether this is due to a torpor or to atony, or to an actual paralysis, it is difficult to determine; in some instances there seems to be an actual tetany of the muscular coats that resist all efforts at relaxation. This may seem fanciful, but it is difficult to explain the phenomena on any other hypothesis. In more than one instance I have given over a pint of castor oil, in repeated doses, and many irrigations before the grave danger was past and the bowel emptied. In such cases I believe that it is just as important to empty the gut as a septic uterus, or any suppurating cavity, no matter how heroic the necessary measures.

I have selected the following cases as types, and I will allude to them as briefly as possible:

CASE I. In August 1906, I was called in consultation to see a child at Deal, New Jersey. I was the fourth physician in the case. The patient had been ill for two days. The attack was ushered in with a violent convulsion and with no rise of temperature. The convulsions had continued, at varying intervals, altogether there had been six seizures, all of them very severe lasting about half an hour. Between the spasms the child had been stuporous and had vomited frequently. Calomel and castor oil both had been admin-

istered, and the attending physician assured me that the intestinal canal was thoroughly emptied. The diagnosis of meningitis had been made and accepted by all three of the doctors. Inspection of the patient showed a very well-nourished child, very pale, stuporous, and aroused only with difficulty. Further examination was prevented by the onset of a convulsion, which began suddenly, with violent general twitching.

I ordered a mustard bath and put in it a Davidson's syringe, and, while the doctor and nurse were bathing the child and dashing ice-water on its head, I inserted the nozzle of the syringe into the rectum and pumped the mustard-water into the bowel for several minutes. After fifteen minutes in the bath the child was wrapped in blankets with an ice bag at its head, the convulsive movements gradually lessening. While I was making preparations for an irrigation, masses of fecal matter began to come away and the child had the largest single movement I ever saw. There must have been more than a quart. It was smooth and well digested, normal in color, and had no unusual odor. I washed out the colon thoroughly later, but little came away. I gave half an ounce of castor oil and advised the rectal administration of 5 grains of chloral. I saw the child on the following day. It had no more convulsions. It was still very stupid and had slight strabismus. The doctor told me that the next irrigation, given in the evening, had brought away much fecal matter of very foul odor. I advised castor oil to be given every five hours and enemata at the same intervals. For three days the foul, green actions persisted, but only with the irrigations. There were no spontaneous movements. The child had a slow convalescence, with insomnia, frequent attacks of colic and great irritability. It was put on malted milk and barley. It has been in good health since, although it has never been able to digest cow's milk except in small quantities.

This case is noteworthy from the very large fecal accumulation that existed in spite of large doses of cathartics. The degree of systemic poisoning was not very profound and not followed by the usual severe enteritis. There was no fever at any time.

CASE II. The second case is an exact antithesis of the preceding one in that the alimentary canal was empty; the amount of toxic material was small and definitely known and the symptoms of poisoning were very unusual.

The child, twenty months old, had had an attack of gastro-intestinal catarrh, which lasted about a week. The case was sent to me from Summit, New Jersey by Dr. Walter James. The illness had been quite severe, but the child was now convalescent. It had had no nourishment for a week except barley gruel and animal broths. It was emaciated, pale and languid. The temperature was 100° F. The only stool that I saw was thin, smooth, with very little odor, just such a discharge as would be expected from such a diet. It was also black from bismuth. The child had little appetite and was very fretful. I ordered an ounce of beef juice, which had to be prepared in the hotel kitchen. The baby took this with apparent relish about 7 P.M. and within an hour had gone to sleep. At midnight, five hours later, I was summoned in a hurry as the baby was acting very strangely. I found it in a condition of wild, almost maniacal, excitement, screaming, throwing itself about in its nurse's arms and wildly calling her name, looking for her all over the room. It was evident from this that the child was blind. It had a wild expression and a very active rotary nystagmus, which the mother told me was new. I took the temperature with difficulty—it was 103° F. The child seemed on the verge of a convulsion. I gave it half an ounce of castor oil and proceeded immediately to wash out the colon. This was a very difficult procedure, owing to the violent movements of the child, whose screaming had increased, arousing the people on the floor. I think the nystagmus was the most violent I ever saw. I passed the tube with some difficulty and had proceeded several minutes with the irrigation when the screaming became less, child became quiet and the nystagmus diminished. The enema brought away very little. In half an hour the child was quiet, but wide awake; it remained greatly excited all night; did not sleep at all. At daybreak five hours later, I was summoned again and found precisely the same condition. Nystagmus had reappeared; child was screaming and throwing itself about as before. Again the irrigation was begun and in a few moments both screaming and struggling subsided and the child became quiet as before. This irrigation brought away considerable mucus and the odor, toward the last, became very foul—that peculiar nauseating smell that always obtains in cases of intestinal toxemia, which is pathognomonic of that condition. I do not remember ever to have seen a case of intestinal intoxication of any severity that did not exhibit this symptom.

This singular condition reappeared every five or six hours during the day, with no abatement in violence. In the afternoon I had the child removed to the Babies' Hospital, two miles distant, as it was impossible to care for it properly in the cramped rooms of a hotel. There the scene was re-enacted for three days, the symptoms gradually subsiding, the interval between the attacks becoming longer and the seizures less violent. Between the attacks the child was wide awake, and did not sleep at all for forty-eight hours, although chloral and bromides were given in considerable doses. A cathartic was given three times a day and an enema whenever the excitement and nystagmus appeared; the foul odor of the discharges gradually became less and, on the third day, the child had short intervals of sleep. During the whole of this time it obstinately refused any nourishment, even water, and fought violently against it. I began, on the first day in the hospital, with gavage, giving it 4 ounces of granum gruel with 2 drams of liquid peptonoids. This was alternated with mutton broth. At the end of a week the nystagmus and screaming attacks had entirely gone, the child was removed to a boarding house in the village near by, and a nurse was sent from the hospital every four hours to give the gavage. At the end of two weeks the child was sent back to its home in Summit; it had gained a pound and seemed well and happy; its stools were normal, but it still absolutely refused to eat. The gavage was continued for two weeks more until the child had gained 3 pounds. It had taken no cow's milk but it had been fed with malted milk, gruels and eggs. At the end of this time I sent for the nurse to come back, and I know nothing more of the history except that the child was starved into submission and has been perfectly well since.

This case illustrates very well how very little poisonous material is needed to set up a very grave infection. Moreover, this infection may reproduce itself rapidly and often for a long time. It shows, also, the danger of preparing food for infants in hotel kitchens. Hotel food, at the best, is always bad for children. No careful record of the cathartics was kept in this case until it reached the hospital. After that, it had a tablespoonful of castor oil about every eight hours, and the irrigations, which were very thorough, by means of a tube passed up through the sigmoid flexure, were given at intervals of every five hours. The toxic

symptoms, nystagmus and insomnia were also rather unusual and in sharp contrast to the stupor of the preceding case.

CASE III. Baby, eight months old. Seen in consultation last July. The child was apparently in collapse, pallid, eyes sunken, lids half opened, fontanel depressed, extremities cold. It had just been brought from the city to Long Branch, with a history of a week's illness consisting of mild diarrhea, occasional vomiting and temperature fluctuating from 100° F. to 102° F. The doctor in charge of the case had given a grain of calomel a few hours previously; this had been followed by a dose of two teaspoonfuls of castor oil. There had been one stool. It was greenish and contained a few shreds of mucus, but otherwise was smooth and not very bad. The child had been fed for two weeks on cow's milk and malt soup, with a history of overfeeding. Its abdomen was flaccid, very soft, and its condition very apathetic. It seemed dazed and cried feebly when violently disturbed. Refused all nourishment, but resisted it feebly; temperature, 99.4° F. I could not come to any conclusion concerning this case until the tongue was examined. I found this absolutely dry, a condition not uncommon in sick children after a journey. I called for water and gave it a teaspoonful, putting it in the corner of its mouth with a dropper. The child took it eagerly and followed the movements of the dropper with its eyes. For fully half an hour I had the nurse give water constantly, and not until it had taken nearly a tumblerful did its thirst seem to be relieved. After this it seemed brighter. In the evening the doctor telephoned me that it was very much better. I concluded that the apparent collapse was due to a loss of water from its blood. The following morning I saw it again. The bowels had moved only once from the purgative; the appearance of the stool was negative, such as one would expect to find from a diet of barley gruel; the child acted more naturally, although it was very irritable; seemed to be in fairly good condition; temperature, 99½° F. I advised the doctor to give a high irrigation, as the purgative had not acted as thoroughly as was expected. I also advised condensed milk to be added to the barley in the proportion of 1 dram to 6 ounces; the child seemed to be convalescing after a mild attack of gastro-enteric catarrh and I dismissed it entirely from my mind. Six hours later I was summoned in haste and found the child

stuporous and again in apparent collapse; condition very like the preceding day except that the tongue was moist and the temperature had risen to 102° F. I washed out the bowels myself, using one of my own tubes, which I was able to pass with little difficulty. After a few minutes masses of white, undigested milk curds began to appear in the escaping water, the first I had seen. The odor, which had not thus far been noticeable, now became exceedingly foul and larger amounts of partially digested milk began to appear. For two days thereafter the enemata were repeated at intervals of four hours, and castor oil was given in half-ounce doses every eight hours. The stools, which were never spontaneous, consisted, during that time, of undigested milk and masses of clear mucus, and the odor persisted. During that time also the child was semi-comatose, and some of the time could not be aroused at all. There was little evidence of catarrhal inflammation in the stools which were mostly half-digested milk. During this time the temperature did not rise above 100° F. Every attempt to give food was resisted; the child would cry feebly for a minute and relapse immediately into a stupor. The pulse became rapid (160), feeble and irregular. The temperature was subnormal. Gavage was begun on the second day—4 ounces of granum gruel and a dram of panopepton every four hours, with half of the white of an egg. This was seldom vomited. On the second day the child's vital condition was so low that I gave 150 cc. of saline solution by hypodermoclysis. This was given at one sitting in four different places, and the procedure was repeated daily. This condition lasted about a week; it took two days to get the old milk curds away, then the granum began to come through in the washing. To my surprise it was fairly well digested. During this time the child was entirely blind, and if the irrigations and castor oil were not given promptly the symptoms would become much worse. The family noticed this, and would frequently ask that castor oil should be given to the child, the beneficial effect of it was so perceptible. At the end of the week it began to brighten up; it would follow bright objects with its eyes and, in its intervals of consciousness, seemed to know its mother and began to pay attention to noises which it had ignored for a week. During this time it lay perfectly limp. The respiration was irregular, often sighing. It had no rigidity during its entire illness, no convulsive attacks, no signs of cerebral

irritation. Another physician, who was called in consultation when I could not come, made a diagnosis of meningitis, which he asserted had obtained from the first. The child gradually improved, condensed milk was added to its granum in proportion of 1 dram to 6 ounces; odor entirely disappeared from the stools; digestion was fairly good. It began to notice much more and looked as if it were going to recover. At the end of the second week I saw it only every other day; the nourishment had been increased to 5 ounces. But the improvement was only temporary—the brain had been too much injured by the severity of the toxemia; hydrencephaloid symptoms gradually reappeared. The child lived three weeks from the time I first saw it, and finally died of exhaustion and heart weakness. During the whole illness it had but two or three spontaneous movements; usually a full dose of castor oil and an enema were required. The appearance of the stools was usually quite good, but toward the last they were occasionally green and contained masses of mucus; the foul odor invariably returned if the oil enemata were not given. Over a pint of oil was given during the illness. The food given by gavage was usually retained. Hypodermoclysis was practiced four times and with no signs of local irritation. Before death I made a Quincke's spinal puncture to satisfy the attending physician that the child did not have meningitis. Up to that time I am sure he had a lingering doubt. About 20 cc. of a perfectly clear fluid was obtained. It came without signs of pressure and remained perfectly clear in a sterile tube for twenty-four hours. There was never any evidence of deep-seated intestinal inflammation. The urine was normal at first but contained a trace of albumin toward the end.

It seems to me this was an unequivocal case of pure intestinal toxemia, with the symptom-complex known as hydrencephaloid, or spurious hydrocephalus. If any autopsy had been possible, I have no doubt it would have shown a condition analogous to the wet brain of drunkards. At any time during the three weeks, if the food had been allowed to accumulate in the intestines, symptoms of deeper toxemia would have appeared at once. Most cases of profound intestinal intoxication lead to subsequent enteritis; in this case there was little or none.

CASE IV. R. S., fourteen months; 8 pounds at birth; nursed by mother eight months. After weaning continued to thrive,

except for occasional mild attacks of intestinal indigestion. These were caused, as I suspected, by the nurse increasing surreptitiously the strength of the formula—a fault that is not uncommon where too much stress is laid upon the weekly gain, and the loss of a few ounces throws the entire household in mourning. Weight at fourteen months, 25 pounds, 5 ounces; food consisted of 7 ounces of milk with 1 ounce of barley gruel in each bottle, five feedings at four-hour intervals. Late in April as the curdy stools increased, the formula was reduced to one-half milk. This did not help matters; stools were still undigested and often very foul; appetite was capricious; there was too much flatus and unusual irritability, which was partly due to teeth. As the first molars were imminent, early in May the milk was reduced to one-third, with no improvement. This was changed to condensed milk, 1 dram to 6 ounces of barley gruel. May 5 the child began to vomit; temperature rose to 101° F. in the morning, 104° F. in the evening; all nourishment stopped except albumin water;  $\frac{1}{4}$  grain calomel every half hour for eight doses, followed by half an ounce of castor oil and thorough irrigation of the bowel. The child became rapidly stuporous; lay with lids half open, eyes rolled up. Did not even rouse thoroughly for the enema. Fought violently against nourishment, even water. No movement resulted from the cathartics, nothing came except with the irrigations. This consisted of foul-smelling milk curds which gradually gave place to green mucus. There was no vomiting after the initial attack. The baby lay in this stupor for ten days. It passed nothing from its bowels except green, foul mucus that looked like seaweed, and this only after large doses of castor oil. The enemata were not even effective unless a preliminary dose of oil had been given. Temperature fell gradually to normal after the third day. A perfectly regular system was adopted—irrigation every four hours, castor oil  $\frac{1}{2}$  ounce to 5 drams every eight hours; nourishment, which consisted of equal parts of broths and barley gruel or panopepton and albumin water, were forced with great difficulty every two hours. The bad odor persisted for a week and the amount of green mucus that came after each irrigation was incredible. It must have been at least half a pint each time. From the beginning the child seemed indeed very sick. The extremities were cold, the pulse was 150 to 160 and weak. Respiration was sighing and sometimes irregular. Strych-

nin (grain 1/200) was given regularly every three hours. At the end of a week there was little change except marked emaciation. Still semi-comatose with occasional fits of screaming, during which it would tear at its face with its nails. If the cathartic and irrigations were not promptly given, all the symptoms were worse—the coma would deepen and the foul odor reappear. The irrigations were very tedious and often took nearly an hour. The long tube was abandoned as the child was too weak and a short tube four inches long used. The child was often held up in an inverted position for several minutes; usually it was necessary to allow the water to run in for twenty minutes before expulsive efforts were induced. May 21, two weeks after the onset there was little improvement in the child's condition. Castor oil was still necessary every twelve hours, irrigation every six hours. Stools still abundant, consisting of mucus with occasional signs of fecal matter; odor entirely gone. Whey had been given, but abandoned for malted milk, 1 dram to 4 ounces of barley or Mellin's food in same proportion with albumin water and panopepton in intervals of feeding. The total quantity of nourishment on this date consisted of malted milk and barley, 15 ounces; albumin water, 7 ounces. Urine abundant, contained trace of albumin. Was still apathetic and stupid most of the time, but had violent screaming attacks and at times seemed maniacal.

On May 22 was taken to the country, after several consultations with Dr. Holt. Dr. A. W. Bingham stayed in the house with it for eight days. At this time it became very puffy in the face and rapidly developed general edema, evidently due to hydremia. Specific gravity of the blood had become so low that osmosis was reversed. Fluid diet was now reduced as much as possible, and food given in form of jelly. By continual scratching and tearing at its face, the skin had become infected and a septic dermatitis spread over the whole face and scalp, closing both eyes and making the child's appearance most pathetic. The first edema subsided slowly, but was quickly followed by a second and worse attack. After this cleared up, the weight, early in July, was 14 pounds, 14 ounces—a net loss of 10 pounds, 7 ounces during the illness. Stools were rarely spontaneous. They were still very bad and often foul consisting of masses of mucus and partially digested food. Sometimes the child would scream for hours at a time, as if insane. Its skin was wrinkled like an old woman's and

covered with scars and patches of erythema and eczema, and it hardly seemed possible that it had vitality and protoplasm enough to carry on the chemistry of life. But I was mistaken. Early in July it had an acute attack of vomiting and high temperature, and I believed the end had come. It lay perfectly still and white, with its eyes rolled up, and mentally I gave up the fight. In despair I gave a grain of calomel and repeated it two hours later. This was followed by a monumental clearing out, and from that moment the improvement began. It was very slow and often interrupted by reverses. It took two weeks to gain the first ounce, and condensed milk was the food that finally succeeded. The baby now weighs 19 pounds and is improving all the time. I am now changing the food to malt soup and cow's milk. Its hair has all fallen out, and it is beginning to find out that it has legs, although still too weak to stand. This is a particularly good example of very grave intestinal toxemia with complete atony of the bowel, and the child was saved only by heroic doses of cathartics and other rigorous methods of emptying the intestinal canal. Over a pint of castor oil was given in the first ten days, and therein lies the crux of the whole matter.

In all intestinal infections cathartics should be given in large doses and at once—all traditions of dosage must be ignored. I could cite many cases like this, and several times I know I have saved life by a bold dose at a critical moment. Even vomiting is not a contraindication. Castor oil is so adhesive that it cannot all be vomited and, if repeated boldly, enough will soon be retained to evacuate the intestine. Calomel is so heavy and insoluble that it is not easily vomited and, if persisted in, will usually act. In my experience of twenty-seven years I have never seen any harmful result from either drug.

#### CATHARTICS

In the foregoing cases it must be remembered that the intestine was unresponsive, ordinary stimulation was of no avail, the gut itself was more or less paralyzed, and the nerve centres were dulled by the toxemia. Calomel is a most useful drug, and I always use it in cases of diarrhea where the bowel is already active. I have heard a well known pediatrician say that it is so harmless that it might be given by the teaspoonful. In my opinion, however, it hasn't sufficient initiative to be always avail-

able, and to depend upon it in serious cases is only losing valuable time. It should always be given in  $\frac{1}{4}$  grain doses, repeated according to the demands of the case. Doses of  $1/10$  of a grain, in my opinion, are useless. Even for infants a few days old  $1/8$  or  $1/6$  of a grain is a better dose. If not effective in two or three hours it should be followed at once by a saline or castor oil. I believe that there would be few serious cases of dysentery if the initial infection were promptly and vigorously removed.

Next to castor oil I like the senna preparations. Salts in solution are preferred by many writers, and are considerably used for this purpose, but it is necessary to use a large quantity of water to dissolve them and the taste is also disagreeable and apt to induce vomiting. The sulphates of soda and magnesia are generally used for this purpose. Sulphate of soda is sparingly soluble in water; the solution in use at the Babies' Hospital contains 15 grains to 2 drams. If any stronger than this it will crystalize. They are very useful in dysentery given in small repeated doses. Milk of magnesia is popular; it is antacid and prompt, especially if given with orange or lemon juice, but it is mild and not to be relied on in serious conditions. Cascara, in aromatic fluid extract, is good but slow, and liquorice powder is one of the best-all-round laxatives in doses of a few grains to  $\frac{1}{2}$  dram, but it is slow. Rhubarb, in syrup or tincture, is useful in mild diarrhea, and has a secondary astringent effect, but, in all serious cases where promptness and certainty of action are indispensable, castor oil is the best, either pure or in the form of laxol. The latter preparation has no taste of castor oil, as it has been disguised by peppermint, but it is very sweet and not so good for continued use. Pure castor oil may be given every few hours for days and it is harmless. I have never seen any ill effects from its use.

#### IRRIGATION

Enteroclysis is an indispensable manoeuvre in all intestinal affections, but I believe that it is often overdone. It is sometimes unnecessary and harmful, and oft-repeated irrigation is rarely necessary. The chief indications for its use are bloody stools and tenesmus, which it will usually relieve. It should be used in all high temperatures, or other emergencies, but after the intestinal canal is thoroughly emptied irrigation should not be

kept up unless it is necessary to relieve pain or remove bacteria or other toxic products that have accumulated in the intestine. In little delicate babies it is dangerous. I have seen it produce shock and serious laceration. It should be remembered that it is always more or less exhausting, and that in ordinary diarrhea, where the products of inflammation are few, it is often meddlesome and dangerous. The technique is not simple; it requires care and practice to do it properly. I generally use a tube made especially for me by Tiemann.

#### FOOD

In my opinion fresh milk should never be used in cases of intestinal toxemia until every trace of infection is gone, and it is my custom to use condensed milk or malted milk, or other of the evaporated milk products for several days after such an attack. A violation of this rule is apt to result in a reinfection, and such a relapse is often more serious than the original attack. Milk seems to be a common carrier for all pathogenic bacteria that infest the alimentary canal. There seems to be no doubt that it is the medium of infection in most cases, whether the poison comes from without or has its origin within. In either case the bacteria thrive and multiply with greater rapidity in the presence of milk, yet there are eminent authorities who hold the opinion that sterile milk is innocuous and may be used in such toxic cases. It is my rule to withhold it absolutely as long as there is any trace of the foul odor that obtains in these cases, and even long afterward. The following brief résumé of two cases will illustrate my experience on this point.

R. S., two years old; in perfect health; digestion normal; had an acute attack; temperature 105°F. Also vomiting, urticaria, delirium. Bowels were moved with difficulty after repeated doses of calomel followed by castoria. Then castor oil was given every four hours, and the bowels were irrigated until the temperature came down. Stools were very foul and consisted of milk curds and masses of mucus. Two days after the temperature had remained normal and the odor disappeared one milk feeding was given, which consisted of 2 ounces of milk to 4 ounces of barley gruel. Within twelve hours after this, the temperature rose to 106°F., urticaria reappeared and the child was very sick; the temperature persisted for several days, fluctuating between 101° F. and

105°F. The child was stuporous most of the time, during which he was seen by Doctors Holt and Jacobi several times, and the diagnosis was in doubt. The persistent foul odor, however, and the recurrent urticaria finally removed all doubt. At the end of a week this second attack had subsided leaving the child in a weak condition from which it did not seem to rally. It had no appetite and was extremely apathetic. Two days later the temperature rose again suddenly to 105°F. There was a suppression of urine and the child died of acute Bright's disease. The urine had been examined during the first attack and found normal. In this case the nephritis was no doubt due to the profound toxemia, and I believe that the second attack and the Bright's disease would not have occurred if the milk had not been given.

J. A. M., twenty months; unusually healthy; weighed 27 pounds; brought in from Princeton on a visit to his grandfather in the city. I was called in during the night and found him with temperature 105°F., twitching a good deal and apparently about to have a convulsion. I gave him a bath at once and washed out the bowels, using the high tube, which brought away a tremendous amount of foul-smelling material. This kept coming away in such quantities that it took me nearly an hour to empty the bowel. The temperature fluctuated for several days, and the child was so sick that I was obliged to sleep in the house one night. I do not remember the minutiae of the case, but it was necessary to administer cathartics and irrigations several times a day, and at the end of a week the boy was quite convalescent, except that the frequent green discharges persisted, and I was obliged to resort to bismuth and an arrowroot diet. One evening, owing to some trouble in the kitchen, the arrowroot gruel could not be made, and we sent to the Home Bureau for a fresh supply. I did not give the order, but supposed, of course, that it was to be made with water and not milk. The boy had one feeding of the Home Bureau supply early in the evening; I think he took 6 ounces. About three o'clock in the morning I was summoned again and found him with a high temperature, nearly 105°F., vomiting, and just as ill as he had been during the initial attack. I was suspicious of the arrowroot gruel and, on examination, found that it had been made with milk. I was fortunate to get him cleaned out more quickly this time, and he recovered more rapidly, although he was very sick. I am sure that this relapse

was not a mere coincidence, I have seen it occur too often, and it is incredible how very little milk is required to set up a reinfection and often serious trouble.

Opinions differ widely as to the proper diet in cases of this kind. As a rule, proteid diet is avoided and the preference given to farinaceous gruels. One pediatrician prefers beef juice and other beef products exclusively, but most authorities are afraid of it and other foods containing proteids. In my opinion, a middle ground is advisable, although I would not hesitate to use broths alone. I prefer a mixture of equal parts of animal broth and cereal decoction. This seems to agree with most cases: Chicken, mutton or veal broth with equal parts of granum, barley or arrowroot gruels. The latter should be made weak, about 2 drams to the pint, and digested with cereo or some other form of diastase. The arrowroot is usually reserved for cases of diarrhea. In acute cases, however, it is much better to give no food at all, simply pure water, or, in cases of vomiting, albumin water, consisting of 1 dram of brandy, white of one egg, and 1 pint of water. Some writers object to this, as it often comes through undigested, but I never could satisfy myself that it produced irritation, and I use it in all cases. All nourishment should be given in small quantities, and interval enough allowed between feedings to permit of digestion, which, under these conditions, is always slow. In cases of very high temperature digestion of course is in abeyance, and all food should be avoided. As convalescence is established I do not hesitate to use malted milk, or condensed milk, the latter for little babies and the former for older children. It should be very weak at first—1 dram to 6, or even 8, ounces. The Eagle brand has been found pure and safe. It is best to get a fresh can every day. Malted milk to be used in exactly the same way. Nestle's food and Eskay's food are also useful in the same proportions. In all cases of disturbed digestion in hot weather, it is my custom to drop milk at once and rely upon one of the above products.

## DEPARTMENT OF ABSTRACTS

*Conducted by*

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ANDREWS, G.C.; DOMONKOS, A. N.; TORRES-RODRIGUEZ, V. M.  
and BEMBENISTA, J. K.: HEMANGIOMAS—TREATED AND UN-  
TREATED. (Journal American Medical Association, 165:1114, Nov.  
2, 1957).

The records of 1,113 patients with the diagnosis of angioma were studied. Of these, 329 patients had hemangioma simplex and 584 had hemangioma cavernosum. Of the 153 patients with hemangioma simplex who received no treatment, 102 could be observed adequately. In 64 cases (63 per cent) the lesions involuted or improved within five years. In 38 (37 per cent) the hemangiomas persisted after five years. In those cases of hemangiomas simplex with spontaneous involution, 83 per cent were lesions with a diameter of 1 cm. or less. It may be concluded that any hemangioma simplex on the face measuring 1 cm. or more should be treated without delay, since those of larger size have poor possibilities of involution without therapy. Occasionally one encounters a case where a large hemangioma disappears spontaneously without scar, but one also sees occasional cases in which large hemangiomas persist, grow, ulcerate, and become serious problems. The likelihood of ulceration of hemangiomas on the lips, nostrils, eyelids, and the ears suggests that these lesions should be treated even though they are less than 1 cm. in diameter. Of the 135 patients with hemangioma cavernosum who received no treatment during the first five years of life and who could be followed adequately, 22 (16 per cent) showed involution or improvement of the lesions within a period of five years. In 113 (84 per cent) these lesions persisted more than five years. The high percentage of persistence in untreated cavernous hemangiomas indicates the desirability of treatment for all cavernous hemangiomas. When treatment is given to hemangiomas, the method of therapy must be carefully chosen to secure the best cosmetic results. We feel that radium therapy, properly administered, assures excellent results without risk of radiation sequelae. However, in

some cases surgical excision, ligation, solid carbon dioxide, or roentgen ray treatment are indicated.

AUTHORS' SUMMARY.

EVERSOLE, S. L., JR.; HOLMAN, G. H. and ROBINSON, R. A.: HITHERTO UNDESCRIBED CHARACTERISTICS OF THE PATHOLOGY OF INFANTILE CORTICAL HYPEROSTOSIS (CAFFEY'S DISEASE). (Bulletin Johns Hopkins Hospital, 101:80, August 1957).

Histological findings of infantile cortical hyperostosis which have not been described previously are presented in this paper. Previously, only non-inflammatory subperiosteal new bone formation has been described. However, it is now clear that in the early stage of Caffey's Disease there is a marked acute inflammatory reaction with many polymorphonuclear leucocytes forming small purulent foci in the connective tissue stroma of the abnormally active periosteum. Osteoid trabeculae appear throughout the overactive periosteum in this acute stage of the disease and during this stage the periosteum as a histologically identifiable structure surrounding the bone is thereby lost. The entire process extends out to invade the soft tissues overlying the periosteum, and in foci the peripheral layers of the original bones are resorbed. In this acute stage a biopsy including only the periphery of the lesion may be mistaken for osteogenic sarcoma. In the subacute stage, the periosteum reforms as a peripherally limiting structure about the old and newly formed bone. In this later stage the osteoid laid down in the acute stage becomes more completely calcified and is "subperiosteal". In a still later stage, or the remodelling stage, the extra bone peripheral to the original bone is removed. The subacute and remodelling stages from the histological viewpoint are the ones which have been previously described in the literature.

AUTHORS' SUMMARY.

PULASKI, E. J. and TALLEY, T. P.: CERVICAL ACTINOMYCOSIS IN A THREE YEAR OLD CHILD. (Antibiotic Medicine and Clinical Therapy, 4:755, Nov. 1957).

An early case of cervical actinomycosis in a three year old child with a 10-day history of sore throat is reported. The diagnosis was established by growth of *Actinomyces bovis* in the second of two aspirates of purulent exudate from the neck. Response to an oral course of tetracycline therapy was complete, and there has been no recurrence. The point of entry of the *Actinomyces* was not established.

AUTHOR'S SUMMARY.

POHOWALLA, J. N. and GHAI, O. P.: TYPHOID ENCEPHALOPATHY IN CHILDREN. (*Indian Journal Pediatrics*, 24:137, May 1957).

One hundred and fifty-five cases of typhoid fever in children have been studied. Fifty-seven cases showed evidence of involvement of the nervous system. Thirteen out of the latter group followed a characteristic clinical pattern of typhoid encephalopathy which is discussed in detail. Typhoid encephalopathy bears a serious prognosis with high mortality and produces neurological sequelae in over half of the cases that survive. Its early recognition and institution of timely and vigorous treatment is stressed.

AUTHORS' SUMMARY.

CHOREMIS, C.; LIAKAKOS, D.; LEKOU, S.; GARGULAS, A. and DROSOS, X. C.: EFFECT OF ISONIAZID AND CORTISONE IN CHILDREN VACCINATED WITH BCG. (*American Review of Tuberculosis and Pulmonary Diseases*, 76:263, August 1957).

BCG was administered intradermally to twenty-four children between the ages of 6 and 11 years. The children were divided into three groups of eight each. One group served as controls. All of the children became Mantoux positive and, on biopsy of the vaccination site, demonstrated typical tuberculous lesions. The second group received isoniazid from the day of vaccination. Three children of this group became Mantoux positive. All of the eight children, however, on skin biopsy, displayed epithelioid cell infiltration of the dermis but absence of caseation and giant cell formation. The third group received both isoniazid and cortisone. Two became Mantoux positive and the entire group, on biopsy, demonstrated only nonspecific lymphocytic infiltration of the dermis. These observations suggest that the inhibitory effect of isoniazid on the development of tuberculous lesions is further augmented by the administration of cortisone.

AUTHORS' SUMMARY.

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Christmas  
lives in the joy  
and satisfaction  
of the giver...



...and in the  
delight and  
thankfulness  
of those  
who receive

Almost everybody remembers

to make Christmas seals a part of his giving...

because they give the greatest gift of all,

Health, life itself, to so many.

How about you?



(YOUR NAME HERE)

## KEY MAN AGAINST CANCER



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